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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/960,665	09/21/2001	Neal Rosen	MSK.P-038-2	5586

21121 7590 07/12/2005

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EXAMINER	
KIFLE, BRUCK	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 07/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/960,665	ROSEN ET AL.	
	Examiner	Art Unit	
	Bruck Kifle, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6,7,12,13 and 15-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 6, 7, 12, 13 and 15-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

This supplemental response is in response to the telephone call received on June 6, 2005 by Applicants representative requesting correction of claim numbers and consideration of the references A-H filed 03/17/03.

Applicant's amendments and remarks filed 12/27/04 (claims amended 4/17/05) have been received and reviewed. Claims 1, 2, 6, 7, 12, 13 and 15-40 are pending in this application.

The rejection of the claims under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement and the rejection over 35 U.S.C. 101, double patenting, are withdrawn.

It is noted that Applicants have the wrong serial number in the heading. Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 1, 2, 6, 7, 12, 13 and 15-40 are again rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the geldanamycin dimers, wherein the linkers are $(CH_2)_{4\text{-}12}$ and linked at the 17-carbon of each geldanamycin, to treat breast cancer, does not reasonably provide enablement for "a chemical compound comprising first and second hsp-binding moieties which bind to the pocket of hsp90 with which ansamycin antibiotics bind, leading to degradation in proteasomes of a subset of proteins requiring hsp90 for conformational maturation, said binding moieties being connected to one another by a linker, wherein the first and second hsp-binding moieties each retain the ability in the chemical compound to bind to the pocket of hsp90 and lead to degradation in proteeasomes of a subset of proteins requiring hsp90 for conformational maturation."

The specification does not enable the skilled chemist to make and use the invention

commensurate in scope with the instant claims. The basis of this rejection is the same as given in the previous office action and is incorporated herein fully by reference.

Determining the compound claimed would require synthesis of millions of compounds and testing each to determine whether the compound falls within the scope of claim 1.

The specification does not provide enablement for the treatment of cancer generally. No compound has ever been found that can treat cancers generally even though massive efforts have been directed towards this end. Since this assertion is contrary to what is known in oncology, proof must be provided that this revolutionary assertion has merits. Nearly all anticancer drugs are effective against only a limited group of related cancers. Therefore, a compound effective against cancer generally would be a revolutionary exception. Applicant is asserting that he succeeded where others have failed. Where extensive efforts have all failed, it is reasonable for the Patent and Trademark Office to require proof that the claimed invention actually works for this specific utility. It is well established that a utility rejection is proper when scope of enablement is not reasonably correlated to the scope of the claims. (In re Vaeck 20 USPQ2d 1439, 1444, In re Ferens 163 USPQ 609).

In re Buting 163 USPQ 689 establishes that even clinical tests showing that a compound found to be useful in the treatment of two types of cancers was not sufficient for a much broader range.

Applicants have submitted references showing that the monomeric compounds 17-allylamino-geldanamycin (17-AAG) and Herbimycin are efficacious in a variety of tumor types. The instant specification at page 8, lines 8-11 lists breast cancer, ovarian cancer, pancreatic cancer and gastric cancer. The evidence presented, however, is not commensurate in scope to the

breadth of the claims. The specification is not adequately enabling for the scope of the compounds claimed to treat cancers generally. Claim 1 requires compounds comprising a first and second hsp-binding moieties with which ansamycin antibiotics bind. The references do NOT disclose compounds that have the second binding moiety required by the claims.

The rejection here is that all of the compounds made are drawn to a narrow group which does NOT give a reasonable assurance that all, or substantially all of them, are useful. The claims are not drawn in terms of a recognized genus but are directed to a more or less artificial selection of compounds.

There is no reason why a claim drawn in this way should not be limited to those compounds which are shown to be both new and useful. An Applicant is not entitled to a claim for a large group of compounds merely on the basis of a showing that a selected few are useful and a general suggestion of a similar utility in the others."

Also, see In re Surrey 151 USPQ 724, regarding sufficiency of a disclosure for a Markush group, and MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the instant pharmaceutical arts. Note in Surrey, in which testing done on a group of homogeneous compounds having the same core was deemed NOT sufficient to support claims to various hetero groups of a much narrower range than is being claimed herein and located at only one position in the formula. The instant scope is enormous, in the billions of compounds, and therefore a few compounds within its scope is not remotely representative of such a scope. See MPEP 2164.03.

The reference provided cannot overcome this rejection.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

Claims 1, 2, 6, 7, 12, 13 and 15-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

i) The nature of the linker is unknown. One skilled in the art cannot say which "linker" is intended. Could any one of a bond, a ring structure, a peptide, a sugar, an antibody, a cyclic peptide, etc. be a linker? In addition, in claim 6, the claim language "length of 4 to 7 carbon atoms" is unclear. Are only alkylenes intended or are Applicants relying on the length of carbon atoms. Appropriate correction is required. The linker should have distinguishing identifying characteristics defined to determine the scope.

iii) The scope of the compounds claimed is undeterminable. The term "bind" in the claims is indefinite. There is no way of knowing whether a given compound would bind. Binding is a process which cannot be observed, merely inferred, which is unreliable. There is no test to determine whether binding is present or not. Furthermore, binding alone is not sufficient to determine the scope of the claims, but binding to the pocket of hsp90 with which ansamycin antibiotics bind is required. Now, the metes and bounds of "ansamycin antibiotic" are not known and the nature of the linker is not known. In addition, hsp90 simply refers to heat-shock proteins with an average molecular weight of 90Kd. This is a family of proteins which consists of Hsp90 alpha and beta, Grp94 and Trap-1. These exist in various mutant forms, and even in these 4, the pockets are not exactly the same.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 6, 7, 12, 13 and 15-40 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3, 4, 6 and 9-34 of copending Application No. 09/937,192. Although the conflicting claims are not identical, they are not patentably distinct from each other because these two sets of claims overlap when, for example, two gelanamycins are linked at their respective 17 positions by 1,4-butanediyldiimino.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle, Ph.D. whose telephone number is 571-272-0668. The examiner can normally be reached Tuesdays to Fridays between 8:30 AM and 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bruck Kifle, Ph.D.
Primary Examiner
Art Unit 1624

BK
July 6, 2005